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REMARKS

Support for the amendment to claim 1 is found on page 5, lines 33-34. Support for new claims 25-27 can be found on page 9, lines 11 - 19. Support for new claim 28 can be found on page 6, lines 12 - 15. Where the description refers to MHC molecules, it also relates to HLA molecules, since human MHC molecules are referred to as HLA molecules (see page 1, lines 24 - 25).

The disclosure was objected to on the basis that it contains embedded hyperlinks. Applicants have amended the paragraph bridging pages 9 and 10 of the specification to remove the hyperlinks.

Claims 1-17, 20 and 22-24 have been rejected under 35 U.S.C. § 112, first paragraph, on the basis that the Applicants had not enabled or provided sufficient written description support for "variants, derivatives or fragments" of MHC molecules. This rejection has been obviated by the amendments above which delete reference to variants, derivatives and fragments.

Claims 1-17, 20 and 22-24 also have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite on several grounds. The examiner asserted that claims 1, 2, 6 and 20 are indefinite in their recitation of "functionally." As this term has been deleted from the claims in the amendments set forth above, this basis of rejection has been rendered moot. Claim 2

also was rejected as indefinite on the basis that although a binding event is insinuated, there is no recitation in the claim that a binding event has occurred. This basis of rejection also has been rendered moot by the amendments to claim 2. The examiner also found that claim 8 was indefinite in its recitation of "a variant." This rejection has been obviated by the cancellation of claim 8 above.

Claims 1-3, 5, 9-11 and 16 have been rejected under 35 U.S.C. §102(e) as anticipated by U.S. Patent 5,948,627, issued to Lee et al. The examiner asserted that the reference discloses a method for the detection of HLA antibodies in which serum from a patient is added to microbeads, each of which presents HLA antigens, and incubating the serum and microbeads for a sufficient time for anti-HLA antibodies to bind to the HLA antigens. He further asserted that the reference discloses the addition of a labeled ligand capable of specifically binding with anti-HLA antibodies bound to the HLA antigens and detecting the presence of labeled ligand bound to the HLA antigens. The examiner stated that the claims read on naturally occurring derivatives and so are anticipated by the reference. This rejection is traversed.

As an initial point, Applicants disagree with the examiner's assertion that the claims as examined read on naturally occurring

derivatives. All molecules specified in the claims were recombinant. As amended, the claims no longer recite the use of "derivatives" and are focused clearly on the use of a recombinant MHC molecule. As the '627 patent clearly does not disclose the use of recombinant molecules, the reference does not anticipate the claims of the present application.

Claims 1-3 have been rejected under 35 U.S.C. §102(e) as anticipated by U.S. Patent 6,528,304, issued to Carosella. The examiner asserted that the reference discloses immunoprecipitating a K562-HLA-G2 cell, a recombinant HLA, with monoclonal antibody W6/32, an antibody against MHC Class I heavy chains (i.e., an anti-HLA molecule) and detecting the monoclonal antibody with a labeled antibody. This rejection is traversed.

The '304 patent discloses the use of a pan anti-MHC antibody, W6/32, in the immunoprecipitation of biotinylated membrane lysates of various cells (see column 5, line 66, to column 6, line 25). This antibody is a non-specific antibody that binds to HLA at a non-polymorphic epitope shared amongst products of HLA-A, B and C loci. A copy of two pages from Bioscience's website, provided herewith, confirms this pan-HLA binding ability of this antibody. Thus, this antibody is <u>not specific</u> for a particular HLA molecule. In contrast, a requirement of each of claims 1-3 is that a recombinant HLA

molecule is used to bind to and detect a specific antibody, i.e. an antibody that is present that binds only to a single, particular MHC molecule. Thus the antibody described in the '304 reference falls outside the definition of antibodies recited in claim 1 and the reference does not anticipate any one of claims 1-3.

Claims 20-24 have been rejected under 35 U.S.C. §103(a) as unpatentable over the '627 patent in view of U.S. Patent 5,420,016. The '627 patent was cited on the same basis that it was cited in the rejection above. The examiner acknowledged that the reference differs from the instant invention in failing to teach packaging the components into a kit, but he asserted that the '016 patent discloses assembling various system components into a test kit and that it therefore would have been obvious to one of skill in the art to package the reagents and components of the '627 patent into a kit. This rejection is traversed.

The significant deficiencies of the '627 patent, i.e., that it does not teach or suggest the use of recombinant HLA molecules, as required by the present claims, were discussed above, and that discussion is equally applicable to the present rejection. The secondary reference cited by the examiner does not compensate for the deficiencies of the primary reference, as it has no relevance to the subject of recombinant HLA molecules.

At best, therefore, the combined teachings of the two cited references might suggest kits using non-recombinant HLA molecules but does not suggest the presently claimed invention. The combined teachings of the cited references thus do not render claims 20-24 obvious.

Applicants respectfully submit that in view of the amendments and discussion set forth above, the pending claims of the application now are in condition for allowance.

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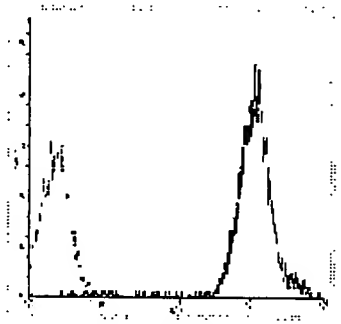
Fluorescein isothiocyanate (FITC) anti-human HLA-ABC

Product Information

Contents: Fluorescein isothiocyanate (FITC) anti-human HLA-ABC
Catalog Number: 11-9983
Formulation: Phosphate buffer pH 7.2, 150 mM NaCl, 0.09% NaN_3, 0.2% BSA
Storage Conditions: Store at 4°C.
DO NOT FREEZE.
LIGHT-SENSITIVE MATERIAL.
Clone: W6/32
Isotype: Mouse IgG2a, κ



Profile of FITC labeled mAb W6/32 (HLA-ABC) staining on human peripheral blood lymphocytes.

Prices for This Product

Cat. No.	Size	Price	Qty	Action
11-9983-71	25 tests	$80	1	Buy
11-9983-73	100 tests	$180	1	Buy

Other Formats of This Product

Cat. No.	Format	Reported Applications
12-9983	PE anti-human HLA-ABC	FC
14-9983	Affinity Purified anti-human HLA-ABC	FC IP
15-9983	PE-Cy5 anti-human HLA-ABC	FC
16-9983	Functional Grade Purified anti-human HLA-ABC	FC

Description

SN 09/890,027

The W6/32 monoclonal antibody reacts with the human major histocompatibility complex (MHC) class I, HLA-A, B, C. MHC class I antigens associated with β2-microglobulin are expressed by all human nucleated cells and are central in cell-mediated immune response and tumor surveillance. W6/32 mAb recognizes a non-polymorphic epitope shared among products of the HLA-A, B, and C loci and immunoprecipitates both 43 kDa and 11-12 kDa chains.

Usage

For research use only, not for diagnostic or therapeutic use. This W6/32 antibody has been reported for use in flow cytometric analysis.

Applications Tested

This W6/32 antibody has been pre-titrated and tested by flow cytometric analysis of human peripheral blood leukocytes. This can be used at 20 µl per 100 µl blood (per million cells).

Related Products

Cat. 11-4729	FITC Mouse IgG2a, K Isotype Control
Cat. 12-9983	PE anti-human HLA-ABC (clone W6/32)
Cat. 14-9983	Affinity Purified anti-human HLA-ABC (clone W6/32)
Cat. 15-9983	PE-Cy5 anti-human HLA-ABC (clone W6/32)
Cat. 16-9983	Functional Grade Purified anti-human HLA-ABC (clone W6/32)

References

Barnstable, C. J., W. F. Bodmer, et al. (1978). "Production of monoclonal antibodies to group A erythrocytes, HLA and other human cell surface antigens-new tools for genetic analysis." Cell 14(1): 9-20.